

# Medical Chemistry and Biochemistry

## Exam Questions 2010/11

### Category 1: Medical chemistry, proteins, enzymes

1. Structure of atom. Chemical bond. Bond energy, valence, electronegativity, covalent and ionic bond, dative (coordinate) bond. Bonds important in organic molecules, single and multiple bonds. Non-bonding interactions (hydrogen bridges, van der Waals forces).
2. Thermodynamics of chemical reactions. Chemical equilibrium, the equilibrium constant, enthalpy, entropy, the Gibbs free enthalpy ( $\Delta G$ ). Reactions exothermic/endothermic, exergonic/endergonic – examples, relationship of  $\Delta H$  and  $\Delta G$ . Relationship between  $\Delta G$  and equilibrium constant.
3. Reaction kinetics, reactions of zero, first, and second order, activation energy, catalysers. Relationship between reaction kinetics and thermodynamics.
4. Dispersion systems. Solutions, ways of expressing their composition (concentration). Activity and activity coefficient. Surface phenomena and adsorption. Chromatographic techniques (gas c., partition c., ion-exchange c. etc.)
5. Dissociation of substances in solution. Solubility of substances, polar and non-polar solvents. Application in biochemistry.
6. Oxidation and reduction. Oxidation number, redox potential, the electrode processes, galvanic cell, relationship of redox potential to  $\Delta G$ , the Nernst equation and its significance in biology and medicine.
7. Water as a solvent and medium. Electrolytic dissociation, self-ionization of water, ionic product of water, pH and its measurement. Hydrolysis of salts.
8. Protolytic reactions. The acid-base concepts, principle of buffering, calculation of pH of strong/weak acid and base, the Henderson-Hasselbalch equation. Importance of buffers in biology and medicine.
9. Diffusion, dialysis, osmotic phenomena, osmotic pressure and osmolality – importance in biology and medicine.
10. What chemical elements the human body consists of? The macrobiogenic, microbiogenic (trace), and toxic elements.
11. Group I and II metals, their most significant inorganic compounds (for human body). Ionic strength. Barium sulfate, gypsum.
12. Heavy metals – toxicological issues, environmental burden. Mechanism of action of a selected heavy metal.
13. Oxides of nitrogen and carbon – biological properties, mechanism of action. Role of oxygen in the organism. Biologically most significant compounds of oxygen and sulfur, description of their structure and function.
14. Trace elements – brief overview and their role in nutrition. Zinc, selenium, copper, iron – description of deficiency states and their causes.
15. Halogens, biologically active compounds containing halogens. Anesthetics containing halogens. Toxic compounds containing halogens.
16. Transition metals – properties, examples of common compounds, biological, medical and toxicological significance. Iron, copper, and zinc in the organism. Ceruloplasmin. Ferritin. Transferrin.
17. Coordination compounds – general properties. Examples of biologically and medically relevant compounds. Chelates.
18. Relationship between structure and properties of organic compounds. Configuration and conformation, types of isomery of organic compounds, mesomery, keto-enol tautomery – examples.
19. Optical isomery and chirality, enantiomer, diastereoisomer, mesoform – examples.
20. Organic reactions important in biochemistry. Types of organic reactions, ionic and radical reactions, their principles and examples.
21. Explanation of esterification, decarboxylation, isomeration, hydrolysis, hydration, hydrogenation, dehydrogenation, Schiff base formation, hydrolysis of esters. Peptidic, glycosidic and anhydride bonds – examples from biochemistry.
22. Alcohols, phenols, ethers, and their sulfur analogues – structure, properties, examples of compounds, significance in biology and medicine. Sulfides and disulfidic bond – examples from biochemistry. Glycerol and its derivatives.

23. Aldehydes, quinones, ketones, amines – structure, properties, examples of compounds, significance in biology and medicine. Hydroxyaldehydes and hydroxyketones.
24. Substances used as disinfectants, mechanisms of action.
25. Carboxylic acids including the fatty acids – structure, properties, nomenclature, examples of compounds, significance in biology and medicine. Relationship to structure of lipids.
26. Substitution and functional derivatives of carboxylic acids, esters, and amides – structure, properties, examples of compounds, significance in biology and medicine.
27. What a functional group is, reactions of functional groups (alcohol, sulfhydryl, carbonyl, carboxyl, and amine) important in biochemistry and laboratory diagnostics.
28. Structural features of L-alpha-amino acids. Optical isomery, ionization at various pH, the isoelectric point. Clasification according to side chain properties, hydrophobic, cyclic, aromatic, thiol, carboxamide, and thioether structures, basic and acidic functional groups. Biochemical significance of these structural properties.
29. Methods of protein study. Physico-chemical properties of proteins useful in their separation – salting-out, denaturation, charge, isoelectric point, utilization of specificity of proteases. Principles of protein separation. Electrophoresis, chromatography, and sequencing.
30. Levels of protein structure. Chemical bonds in proteins. Domain, module, subunit.
31. Structure, function and regulation of hemoglobin and myoglobin. Comparison of structure and function of both proteins.
32. Significance of non-covalent interactions and conformational changes of proteins in controls of biochemical and biological processes. Examples.
33. Regulations of protein function by covalent modification and conformational change. Types. Examples.
34. Monosaccharides: origin and occurrence in nature, biological and physiological significance. D- and L- series, optical activity, types of isomery of monosaccharides. Reactions of monosaccharides and their usage in clinical biochemistry. Glycation of proteins.
35. Saccharides: classification, structure, biological and physiological significance, occurrence in nature. Structure and function of starch and glycogen. Chemical reactions of di-, oligo- and polysaccharides, sugars reducing/non-reducing, O- and N- glycosidic bond, its synthesis and cleavage, specificity of glycosidases.
36. Lipids. Classification of lipids according to their structure. Products of lipid hydrolysis and their significance.
37. Fatty acids. Properties, classification, significance. Essential fatty acids. Basic compounds derived from fatty acids.
38. Enzymes as biocatalysers, specificity to substrate and effect. Relationship of activation energy and change of free enthalpy to mechanism of catalysis. Physico-chemical effects on enzyme activity (pH, temperature, activators and inhibitors). Enzyme nomenclature and classification (EC classes), examples.
39. Structure of enzyme molecule. Multienzyme complexes and multifunctional enzymes. Allosteric enzymes.
40. Mechanism of enzyme action, enzyme-substrate complex. Types of enzyme reactions – one- and multi-substrate reactions. Mathematic and graphic expression of enzyme activity.
41. Kinetics of enzyme reactions, zero order kinetics, initial velocity, maximal velocity, units of enzyme activity. The Michaelis constant, competitive and non-competitive inhibition.
42. Multiple enzyme forms, isoenzymes. Significance of estimation of enzymes in clinical medicine (from practical lessons).
43. Coenzymes of oxidoreductases. One- and two-electron transfer. Relationships to vitamins. Oxidoreductases with heme prosthetic group.
44. Coenzymes of carboxylation and decarboxylation reactions – relationship to vitamins. Oxidative decarboxylation and other types of decarboxylation – roles of thiamine diphosphate and pyridoxal phosphate. Carriers of one-carbon fragment: tetrahydrofolate and its antimetabolites. Relationship of tetrahydrofolate and vitamin B12.
45. Mechanisms of regulation of enzyme activity at the level of enzyme synthesis and enzyme molecule.

### **Category 2: Metabolism**

46. Material and energetic features of metabolism. Anabolic, catabolic, and amphibolic reactions – examples. Coupling of exergonic and endergonic processes in the metabolism. Relationship of  $\Delta G$  to equilibrium constant and osmotic work. Dynamic equilibria of open biological systems.
47. Biological redox processes and their significance for metabolism. Relationship of  $\Delta G$  to redox potential. Anaerobic and aerobic oxido-reduction, comparison of energetic efficiency.

48. The respiratory chain of the inner mitochondrial membrane. Reducing equivalents: what it is, cellular sources, shuttles. Inhibitors of cellular respiration.
49. Conservation and transfer of chemical energy in the cell. High-energy phosphates. Phosphorylation anaerobic (at the substrate level) and aerobic.
50. The chemiosmotic theory of oxidative phosphorylation in mitochondria. Protonmotive force, structure and function of mitochondrial ATP synthase. The respiratory control, effect of uncouplers. Thermogenin.
51. The citric acid cycle: reactions, energetic yield, inhibitors. Anaplerotic (filling-up) reactions of the cycle.
52. Amphibolic character of the citric acid cycle, relationships to other metabolic pathways. Irreversible reactions of the cycle. Regulation of the cycle in response to cellular energy needs.
53. Glycolysis: reactions, localization to organs and subcellular compartments, energetic balance, regulations.
54. Gluconeogenesis: localization to organs and subcellular compartments, energetic balance, regulations.
55. Metabolism of glycogen and its regulation. Hydrolytic and phosphorolytic cleavage of glycosidic bond.
56. Regulation of glucose metabolism. Fate of glucose in the body, its absorption, transport, uptake by cells, role in metabolism of other nutrients.
57. The pentose phosphate pathway, its energetic and metabolic significance. Pentosuria. The uronic acid pathway (overview), relationship to the pentose cycle, role of glucuronate in metabolism of glycosaminoglycans and conjugation reactions.
58. Metabolism of galactose, fructose, lactose and sucrose. Absorption of galactose and fructose, entry to cells. Interconversions of glucose, fructose, and galactose. Disorders in metabolism of galactose and fructose.
59. Structure of glycosaminoglycans, most important examples, occurrence in the body. Proteoglycan complexes. Secretory and membrane glycoproteins. Metabolism of aminosugars and glycosaminoglycans, disorders of their degradation (mucopolysaccharidoses). Sialic acids and their function.
60. Biosynthesis and degradation of fatty acids. Beta-oxidation, fatty acid synthase. Production and utilization of ketone bodies. Energetic balance of their metabolism.
61. Cholesterol: structure, significance in the body, biosynthesis, further conversions, excretion. Transport of cholesterol in plasma. Cholesterol in the diet. Effect of statins.
62. Bile acids: Structure and function, origin, metabolic significance. Primary and secondary bile acids, conjugation. Enterohepatal circulation.
63. Conversion of cholesterol to steroid hormones (corticosteroids and sex hormones). Characteristic reactions of these conversions. C17 and C21 oxidation. Inactivation of steroid hormones.
64. Lipoproteins: characteristics, classes, composition, techniques for separation. Apoproteins: classification, significance, biosynthesis. Metabolism of particular lipoprotein classes. Enzymes that process lipoproteins. Receptors for lipoproteins. Relationship of lipoproteins to atherosclerosis.
65. Phospholipids and glycolipids (cerebrosides and gangliosides). Structure, biosynthesis, degradation. Disorders of enzymes that cleave gangliosides.
66. Transamination, oxidative and non-oxidative deamination, decarboxylation of amino acids. Significance of these reactions. Cofactors of these reactions.
67. Origin and fate of ammonia in the organism. The urea cycle. Role of glutamine.
68. Final products of nitrogen catabolism in humans: urea, uric acid, ammonia. Preference of urea as the main catabolite: advantage/disadvantage, comparison to other organisms.
69. Conversions of carbon skeletons of amino acids. Amino acids glucogenic, ketogenic, dispensable and essential.
70. Synthesis and further conversions of glutamate and aspartate. Relationship to the citric acid cycle and metabolism of proline, arginine and histidine. Function of glutamic acid, its derivatives and analogues in the central nervous system (GABA, excitotoxicity). Glutamate dehydrogenase reaction, synthesis and degradation of glutamine.
71. Metabolism of sulfur-containing amino acids. Degradation and synthesis of cysteine. Degradation of methionine and its synthesis from homocysteine. Active methionine. Metabolic disorders, homocysteinemia. Formation of taurine and sulfates.
72. Metabolism of serine and glycine. Transfer of C1 fragments by tetrahydrofolate. Creatine, choline, oxalates, glycine conjugates, relationship to porphyrin biosynthesis.
73. Metabolism of aromatic amino acids phenylalanine and tyrosine. Hydroxylation of phenylalanine. Formation of melanins. Disorders of metabolism of aromatic amino acids: phenylketonuria, alkaptonuria, albinism.

74. Conversion of tryptophan. Overview of the main catabolic pathway. Origin of serotonin and melatonin, nicotinic acid. Disorders of tryptophan absorption. Bacterial products made from tryptophan. Derivatives of tryptophan in urine.
75. Biosynthesis and degradation of porphyrins.
76. Biosynthesis and degradation of pyrimidines, regulation and disorders, inhibitors of these pathways as chemotherapeutics. PRPP, OMP, carbamoyl phosphate. Thymidylate synthase. Origin of deoxyribose.
77. Metabolisms of purines. Biosynthesis of purine bases and nucleotides, its regulation. The salvage pathway. Catabolism of purines and its disorders. Inhibitors of these pathways as chemotherapeutics, allopurinol. Uricemia. PRPP.

### **Category 3: Molecular and cellular biology, immunochemistry**

78. Bases in nucleic acids, their tautomerism. 'Minor' bases. Nucleosides and nucleotides, structures, nomenclature and abbreviations. Biochemically important mononucleotides and their synthetic analogues. Bonds in polynucleotide chain, its polarity. Non-bonding interactions in DNA molecule. Denaturation of DNA, stability of DNA at various pH. The Sanger's technique of DNA sequencing.
79. Primary, secondary and tertiary structure of DNA. Methods of study of these structures. Organisation of eukaryotic DNA sequences. Stereochemistry of DNA, super-helix, topoisomerases. Chemical composition of chromosome, histones and non-histone proteins. Nucleosomes.
80. Biosynthesis of DNA. Types of DNA polymerases, their specificity, polymerase and nuclease activity. Mechanism of chain elongation, replication and repair enzymes, importance of DNA repair. Inhibitors of DNA synthesis. Topoisomerases, helicases, DNA ligase. Primer, semidiscontinuous synthesis of DNA.
81. Primary, secondary and tertiary structure of RNA. Stability of RNA compared to DNA. Structure and function of particular kinds of cellular RNA.
82. Biosynthesis of RNA, types of RNA polymerases, mechanism of chain elongation. Degradation of RNA, nucleases, their specificity and classification. Inhibitors of transcription.
83. Differences in synthesis of nucleic acids and proteins, and in expression of genetic information in general, between eukaryotic and prokaryotic organisms. Mitochondrial genome and its expression.
84. Post-transcriptional RNA processing. Types of modifications and their significance. Mechanisms of splicing. Ribozyme. Exon, intron. 5'-cap, polyadenylation.
85. Protein-DNA interactions, transcription factors, their DNA-binding domains, and trans-activating domains. Zinc fingers, leucine zippers, nuclear receptors.
86. Gene manipulations, recombinant DNA technology. Restriction endonucleases, vector, gene cloning, transfer of gene into cells. Biochemical problems in expression of recombinant proteins (e.g. production of somatostatin, insulin). Usage of short-interfering RNA (siRNA).
87. Molecular hybridization of nucleic acids. Principle of binding, denaturation of DNA, T<sub>m</sub>, utilization of hybridization in molecular diagnostics. Southern and Northern blotting. PCR.
88. Strategy of replication and gene expression of various types of viruses. Early and delayed RNA. RNA-dependent RNA polymerase, reverse transcriptase. Life cycle of retrovirus.
89. The genetic code. Codon, anticodon, initiator, terminator, degeneracy of the code, its evolution.
90. Effects of antibiotics and chemotherapeutics on the process of expression of genetic information. Reactions that are affected.
91. Mechanism of protein synthesis in the ribosomes. Steps. Possibility of chemical alteration (antibiotics).
92. Regulation of the gene expression at the level of mRNA processing (alternative splicing) and translation (regulation of proteosynthesis). MicroRNA (miRNA).
93. Post-translational processing of proteins, types, examples, significance. Covalent modifications of proteins, types and significance. Difference between glycosylation and glycation. Protein folding. Intracellular control and removal of misfolded proteins: chaperones and proteasome.
94. General principles of cell signaling. Properties of receptors. Signaling molecules, their synthesis, degradation, activation, deactivation, and role in signaling pathways.
95. G-proteins: types, structure and function. Principle of regulation of G-protein activity, GTPase activity.
96. The basic cellular signaling pathways: cAMP, phosphatidylinositols, calcium, Ras/MAPKinases, connection to transcription factors.

97. Projects of human genome sequencing, results and impact. Structure of human genome based on sequencing, classification of human genomic DNA according to function and repetitiveness. Transposons.
98. Vesicular transport. Biochemical and signaling processes in the Golgi apparatus and vesicular system of the cell.
99. Transport across biological membranes. Endocytosis, diffusion, carrier-mediated transport, active transport, sources of energy for transport (ATPases).
100. Structure of biomembranes: Structure of membrane lipids. Significance of membrane components for membrane fluidity. Bipolarity of lipid bilayer. Proteins in biomembranes: interactions with membrane lipids, structure of receptors and receptor-gated ion channels. Antigenic determinants of biomembranes (glycolipids and glycoproteins).
101. Chemistry of cytoskeleton. Molecular motors. Cytoskeleton and cell polarity, cell migration. Importance of cytoskeleton for neuronal function.
102. Chemical structure and metabolism of extracellular matrix. Biosynthesis and structure of collagen. Proteoglycans of connective tissue. Biochemistry of ossification. Molecular structure of basal laminas: proteins and proteoglycans.
103. Regulation of the cell cycle. Cyclins and CDK. Relationship of CDK to cellular signaling network. Phases and check-points of the cell cycle.
104. Molecular basis of tumor formation. Oncogenes and tumor suppressor genes, epigenetic changes (e.g. demethylation of promoters), relationship to cell cycle regulation and apoptosis. Chemical procarcinogens and carcinogens – examples, structure, mechanisms of their effects on expression of genetic information.
105. Mechanisms of initiation and propagation of apoptosis. Difference between apoptosis and necrosis, caspases, bcl proteins, role of mitochondria in apoptosis.
106. Molecular structure of cell junctions (tight junctions, adherens junctions, desmosomes, gap junctions, hemidesmosomes) and cell adhesions (focal adhesions): adhesion proteins, anchoring proteins, cytoskeletal proteins integrated to cell junctions, role of calcium in cellular adhesion.
107. Post-synthetic distribution of proteins in the cell – protein sorting and targeting. Signal peptide.
108. Classification and structure of immunoglobulins. Myeloma proteins, monoclonal antibodies. Relationship of immunoglobulins to the complement.
109. Reaction of antigen with antibody. Types of antibody reaction (agglutination, precipitation, lysis). Quantitative immunoprecipitation and immunoprecipitation in gels. Binding antibodies as the basis of quantitative immunochemical analysis (RIA, ELISA).
110. Generation of antibodies in the body. Clonal-selection theory. Origin of antibody diversity.

#### **Category 4: Essentials of physiological and clinical biochemistry**

111. Prostaglandins, prostacyclins, thromboxans, leukotrienes. Relationship to essential fatty acids and membrane phospholipids. Phospholipase A2, cyclooxygenase and 5-lipoxygenase. Effects of corticosteroids and acetylsalicylic acid.
112. Classification of hormonal receptors according to mechanism of signal transduction (G-protein coupled, tyrosine kinases, nuclear receptors), examples of hormones signaling through each receptor type.
113. Hormones of hypothalamus (statins and liberins) and neurohypophysis (posterior pituitary): chemical nature, biosynthesis, secretion, molecular mechanisms of effects on target cells, metabolic inactivation.
114. Hormones of adenohypophysis (anterior pituitary): chemical nature, biosynthesis, secretion, molecular mechanisms of effects on target cells, metabolic inactivation.
115. Hormones produced by follicular cells of thyroid gland: chemical nature, biosynthesis, secretion, transport in blood, molecular mechanisms of effects on target cells, metabolic inactivation. Graves disease, cretinism.
116. Hormones regulating exchange of calcium (parathyroid hormone, calcitonin, calcitriol): chemical nature, biosynthesis, secretion, transport in blood, molecular mechanisms of effects on target cells, metabolic inactivation. Avitaminosis D (rickets). Alkaline phosphatase in disorders of calcium homeostasis.
117. Hormones of pancreas (insulin and glucagon): chemical nature, biosynthesis, secretion, molecular mechanisms of effects on target cells, metabolic inactivation. Effect of insulin on glucose uptake and utilization, effect on lipolysis. Diabetes mellitus as an example of metabolic disorder. Importance of biotechnological production of recombinant insulin.

118. Hormones of adrenal cortex (glucocorticoids and mineralocorticoids): chemical nature, biosynthesis, secretion, transport in blood, molecular mechanisms of effects on target cells, metabolic inactivation.
119. Hormones of adrenal medulla: chemical nature, biosynthesis, secretion, molecular mechanisms of effects on target cells, metabolic inactivation. Final products of metabolism of catecholamines and pheochromocytoma.
120. Kidney as endocrine organ. Erythropoietin, system renin-angiotensin-aldosterone, calcitriol.
121. Hormones of ovaries (estrogens and gestagens) and testes (androgens): chemical nature, biosynthesis, secretion, transport in blood, molecular mechanisms of effects on target cells, metabolic inactivation.
122. Hormones of placenta: estrogens, gestagens, and proteohormones. Significance of hCG examination.
123. Significance of hormonal feed-backs in the endocrine systems hypothalamus – anterior pituitary - distal endocrine glands.
124. Differences in metabolism in the fed state and during starvation. Relationships between metabolism of saccharides and lipids. Sources of metabolic energy during starvation. Production of ketone bodies.
125. Nutrition: essential amino acids, essential fatty acids, vitamins. Examples of avitaminoses.
126. Inorganic elements and compounds as essential components of nutrition.
127. Digestive enzymes and transport systems in the digestive tracts. Overview of the digestive enzymes for particular nutrients, their specificity. Digestion in the stomach and small intestine. Brush border of intestinal cells and its enzyme outfit, absorption of nutrients (transport across membranes). Biochemical processes in the large intestine.
128. Biochemistry of muscle contraction. Ultrastructure of muscle filaments. Troponin, tropomyosin, actin and myosin. Mechanism of contractile function of muscle fibers, regulation by Ca<sup>2+</sup> ions. Role of ATP and creatine phosphate. Specific features of metabolism in the skeletal muscle (red and white fibers), myocardium, and smooth muscle.
129. Liver: specialized metabolic functions, metabolism of bile pigments, detoxication functions. Biochemical markers of liver damage.
130. Biochemistry of neural synapse. Transduction of excitation at the synapse. Mechanism of neurotransmitter release. Classification of neurotransmitters. Acetylcholine receptors: mechanism of action, classification, agonists and antagonists. Acetylcholine esterase and its inhibitors.
131. Ligand-gated channels, voltage-operated channels. Modulators of neurotransmission. Methods of study and pharmacological dissection of receptors and ion channels.
132. Catecholamines as neurotransmitters, biosynthesis and degradation, examples of agonists and antagonists. Types of adrenergic receptors. Amino acids and their derivatives as excitatory and inhibitory neurotransmitters.
133. Biochemistry of vision. Retinal, transducin, the Wald cycle.
134. Proteins in blood plasma: origin, classification and function. Albumin, transferrin, ceruloplasmin, fibrinogen, immunoglobulins, lipoproteins, prothrombin.
135. Glycemia and mechanism of its regulation. Glycosuria, ketonuria. Glycated proteins. Estimation of glycemia in serum, oral glucose tolerance test. Estimation of glycated proteins in serum. Estimation of glucose and ketone bodies in urine.
136. Bile pigments in blood and urine. Structure, origin, transport and conjugation of bilirubin. Methods of estimation of bile pigments in serum and urine, reference values.
137. Acid-base balance. Metabolic sources of protons, buffers of blood, the Henderson-Hasselbalch equation, molecular mechanisms of acid-base balance maintenance in lungs and kidney.
138. Metabolism of red blood cells: specific features, source of energy, proteosynthesis, role in acid-base balance.
139. Biochemistry of blood vessel wall. Biochemistry of endothelium. Synthesis of nitric oxide (NO), isoenzymes of NO synthase, functions of NO in the body.
140. Biochemical mechanism of blood clotting. Mechanisms of actions of anticoagulant drugs. Analogy with other biochemical processes (protease activation, the complement cascade).
141. Urine, its production and composition. Transport systems in renal tubules. Function of the kidney in acid-base balance and maintenance of blood osmotic pressure. Detection of pathological components of the urine. Estimation of creatinine in serum and urine, clearance of creatinine.
142. Metabolism of exogenous substances. Basic biotransformation reactions – examples. Cytochrome P450. Types of conjugation reactions. Activation of pro-carcinogens.

At the oral examination student chooses by chance one question from each category.